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BY SPECIFIC TREATMENT;
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BY

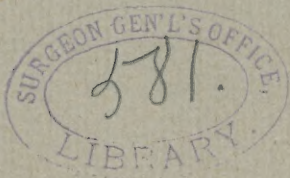
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A CASE OF ASTHMA AND
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MARKED EXCESS OF OXYPHILES IN THE BLOOD.

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THE following case was seen in the heart, lungs, and throat class at the dispensary of the Presbyterian Hospital:

L. S., a girl, aged sixteen years, born of German parents in the United States, admitted January 26, 1897, complaining of asthma and swelling of arms.

Family History.—Mother and one brother living and healthy; father died of exposure to heat at forty-seven years; one brother died in infancy. No history of tuberculosis or cancer in families of parents; no neurotic taint. No information pointing to syphilis in parents was elicited.

Past History.—Always strong and healthy; has grown very fast the last two years; had an acute attack of some disease associated with œdema of legs and body at five years of age; measles the only other disease of childhood. Her brother and herself, when quite young,

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suffered from some pustular affection of the skin of the face. Never had a general eruption; has always suffered from coryza; never ozænic, however. Catamenia have not yet appeared. Has never suffered from sore throat.

Present Illness.—"Caught cold" six months before admission here. This soon developed into typical asthma, with nocturnal attacks of sudden onset, ending in violent paroxysms of coughing with scanty viscid expectoration. These attacks have persisted to date, occurring in the daytime as well as at night, and the expectoration has gradually become more purulent and copious. Hoarseness manifested itself four months ago. This has steadily progressed, and at present voice is only a piping whisper. First noticed enlargement of palms and backs of hands two months ago. This progressed steadily and rapidly, involving the forearms and upper arms as high as the middle of the biceps muscles. The fingers have never been swollen, but have been cold and blue from the first. Very little pain any time in arms or hands, and no redness, tenderness, or heat. On the contrary, the hands and arms have been cold and blue since first appearance of swelling. No involvement of wrist or elbow joints, but she says she can not straighten the fingers.

Appetite has been good. No constipation or diarrhoea. No disturbance of digestion. Suffers at times from typical unilateral migraine with left-sided hemianopia and nausea. Eyesight at other times good. No abnormal frequency of micturition.

Present Condition.—Rather sparsely nourished; distinctly anæmic; tall for her age; face rather long; nose slender, not flattened; expression bright; face a little cyanotic, lips quite markedly so; upper lip a little thickened and tumid; teeth slightly irregular, but well formed, and giving no suggestion of Hutchinsonian teeth. Small scar at right angle of mouth; several whitish linear scars on inside of cheeks and soft palate. Examination of throat by Dr. Bell (class head) showed pharynx to be normal; larynx small and infantile; cords somewhat anæmic; no inflammation or new growth; voice almost lost; tongue

clean; temperature normal; pulse, 24 to the quarter, soft, full, and regular in force and rhythm; no thickening of vessel wall; well sustained. Corneæ clear. Ocular reactions normal. No contraction of fields of vision.

Over left parietal bone, just above the level of the ear, a small nodular swelling the size of half an English walnut. A similar swelling, but smaller, over right parietal bone. These were immovable and painless. No other enlargements of bones discovered. No cervical scars. Chest well formed, symmetrical. Expansion good and equal. Percussion note somewhat hyperresonant throughout. On auscultation, the expiratory murmur was found to be prolonged. Typical asthmatic râles and rhonchi, both medium and coarse, heard with both inspiration and expiration. Vocal resonance and fremitus apparently normal.

Heart: Apex beat in fifth space inside nipple line. Area of cardiac dullness (relative and absolute) normal. Sounds clear at apex and base. Slight relative intensification of second sound over pulmonic cartilage.

Examination of abdomen negative. No enlargement of liver or of spleen. Reflexes normal. A few small discrete glands felt in each groin. No enlargement of axillary, epitrochlear, post-cervical, or occipital glands.

Skin everywhere clear. No scars or discolorations on shins or elsewhere.

Symmetrical enlargement of hands and arms, from metacarpo-phalangeal joints to a point corresponding to the middle of the biceps muscles. Circumference of right wrist, eight inches and a half; of right forearm, just below elbow, twelve inches and a half. Skin of hands and arms cold and blue. Fingers also cold and bluish, but not swollen. Movements of wrist and elbow joints unimpaired. Fingers can not be straightened at the metacarpo-phalangeal joints, owing to swelling of hands.

Sensation impaired at metacarpo-phalangeal joints; elsewhere normal. Bones of hands, forearms, and upper arms apparently uninvolved. No pitting on pressure.

The sensation given to the examiner's fingers was

that of an infiltration beneath the skin and in the muscles. Skin not thickened; freely movable. This apparent infiltration was to be well made out at upper limit of swelling, where the difference in consistence of the involved and uninvolved portions of the biceps muscles was most striking.

Examination of the blood showed the following: Red corpuscles, 3,911,000 per cubic millimetre; leucocytes, 8,300 per cubic millimetre; hæmoglobin (von Fleischl), sixty-eight per cent.

Fresh specimens showed a quite well-marked pallor of the centres of the red corpuscles, and also the presence of an unusually large proportion of oxyphilic leucocytes (eosinophiles), easily recognized by the coarse, highly refractive granulations in their protoplasm. Dried and stained specimens, taken at the same time, showed the same central pallor of the red corpuscles. No variations from the normal in size or shape of the red corpuscles (poikilocytosis and schizocytosis). Several nucleated red corpuscles (normoblasts) and a fair number of polychromatophilic red corpuscles observed. The significance of these abnormal forms will be discussed later. Fully one half the leucocytes were seen to be oxyphilic, presenting a very striking picture. No abnormal forms of leucocytes seen. A differential count of one thousand leucocytes showed the various forms to be present in the following proportions:

Multinuclear, 36.1 per cent.; lymphocytes, 5.1 per cent.; large mononuclear, 5.2 per cent.; oxyphiles, 53.6 per cent.

Patient was given a cough mixture containing ten grains of iodide of potassium and one drachm of fluid extract of euphorbia in each dose, to be taken three times a day. Told to send urine and sputum.

Urine clear, yellow, no sediment. Specific gravity, 1.021. No albumin, sugar, or diazo reaction. Microscopical examination negative.

Sputum: A specimen of sputum expectorated immediately after an asthmatic attack showed typical small vis-

cid masses which, when unrolled on black glass, showed Curschmann's spirals. Over one half the leucocytes entangled in the meshes of the spirals were oxyphiles. A few crystals, corresponding to Charcot-Leyden crystals, observed. Examination of the more purulent morning sputum for tubercle bacilli was negative.

Patient's asthma improved somewhat during the next nine days; no reduction of enlargement of arms and hands.

On February 4th patient was put on "mixed treatment": a thirty-second of a grain of hydrarg. bichlorid. and fifteen grains of iodide of potassium. When next seen, February 16th, the greatest improvement had taken place. Asthma had almost disappeared. Only an occasional râle heard at bases on deep inspiration. Enlargement of arms had entirely disappeared, the palms and backs of hands being still somewhat swollen, giving them the appearance of being cushioned. Circumference of right wrist, five inches and three quarters; circumference of right forearm below elbow, eight inches and a quarter. Bones and skin apparently perfectly normal. Patient states that skin of arms has itched violently a dozen times since last visit, and that there was great diminution in size of arms after each attack of itching. The nodular swellings on parietal bones were hardly perceptible. Voice still piping, but by an effort she could speak in an almost normal tone.

Blood: Red corpuscles, 4,221,000 per cubic millimetre; leucocytes, 7,400 per cubic millimetre; hæmoglobin, seventy-five per cent.

Examination of fresh and stained specimens showed the pallor of red corpuscles to be less.

Only one nucleated red corpuscle observed, and only a few polychromatophiles. Oxyphiles still present in large number. Differential count showed proportions to be: Oxyphiles, 38.2 per cent.; other forms, 61.8 per cent. Four fresh specimens were allowed to dry on the slide, and search was made for Charcot-Leyden crystals, but only one doubtful example was found. When the

patient was last seen her hands were still somewhat swollen, but less so than on February 16th. No asthma.

Blood: Red corpuscles, 4,636,000; leucocytes, 7,600; hæmoglobin, eighty-six per cent.

Microscopical examination showed the condition of the blood to be vastly improved. Pallor of red corpuscles not at all marked. No nucleated red corpuscles or polychromatophiles. The oxyphilic leucocytes were still present in great numbers, as shown by the following count: Oxyphiles, 33.9 per cent.; other forms, 66.1 per cent.

The case above reported is most interesting for several reasons. It was difficult to account for the swelling of the arms, and at first sight it seemed probable that the swelling should be classed under the head of the angio-neurotic œdemas. Pure bronchial asthma is probably a reflex neurosis, and the association with it of a "blue cedema" of angio-neurotic origin is not an unlikely occurrence. The absence of pitting and the irregular distribution of the œdema favored this view. On the other hand, the persistence of the swelling and the gradual onset and progression upward were not characteristic of angio-neurotic cedema, which tends to vary in amount and position, and to manifest itself to its full extent at once. The possibility of the enlargement being allied to the brawny œdemas resulting from chronic passive congestion was considered, but rejected because of the absence of other signs of interference with the pulmonary circulation, such as enlargement of the right side of the heart, albuminuria, etc. The possibility of its being syphilitic was not thought of at first, the only objective signs pointing to such a diagnosis being the nodular swellings on the parietal bones and the linear scars in the mouth. These furnished the clew, and sug-

gested the trial of specific treatment. The patient had never noticed the nodular swellings, and thought they had been there always. Considerable stress has of late been laid upon the presence of linear scars on the inner surface of the cheeks as diagnostic of syphilis. They are supposed to result from the cracking and excoriation of mucous patches. The prompt reaction to specific treatment makes it probable that the enlargement was due to a syphilitic infiltration of the muscles and of the subcutaneous areolar tissue. We are not justified, however, in stating positively that the case is syphilitic; and, moreover, it may be that, and the cedema still be angio-neurotic, the nervous supply of the vessels being involved by the syphilitic process.

Another case, apparently similar to the one above reported, was seen at the dispensary a day or two later. The girl undoubtedly had hereditary syphilis, the facies being characteristic, and a history of syphilis in the parents being obtained. Her arms and hands were symmetrically enlarged, the fingers being also involved, and the skin of the hands and arms being cold and blue. In this case, however, questioning elicited the fact that her arms and hands had been swollen since childhood as a result of frostbite.

The condition of the blood in this case is sufficiently interesting to warrant our going into the subject at some length.

The blood shows marked oxyphilia, with distinct chloroanæmia and evidence of new formation of red corpuscles. These two conditions will be considered separately. It would take up too much space to enter here into a discussion of the various forms of leucocytes in the blood and their "specific" granulations. Those interested

in the subject are referred to the various recent textbooks upon the morphology and pathology of the blood. Cabot's *Clinical Examination of the Blood* is the best book on the subject in English. The same classification into four forms, as was adopted in my article *The Blood Corpuscles in Diphtheria* (1), is utilized here. Those interested in the question of technique are also referred to that article.

It is enough to say that the so-called oxyphilic leucocytes, or eosinophiles, are cells about twice the size of the red blood-corpuscles, with polymorphous nuclei and protoplasm containing a number of large, coarse, highly refractive granules. These granules, when seen in fresh specimens, are greenish and resemble fatty particles. They are neither fat nor hæmoglobin, as is shown by their insolubility in ether and in water. They contain iron (Barker) and are probably albuminous. They have a strong affinity for stains in which the coloring principle is an acid—such as eosin, acid fuchsin, aurantia, etc. To this fact are due the names “oxyphiles” and “eosinophiles.” The stains above referred to are not in reality acid in reaction, being neutral salts; it is simply that the staining power is due to the acid radicle of the salt. This form of leucocyte is not numerous in normal human blood, its proportion to all other forms being a half to one per cent. It is supposed by most authorities to be the last step in the development of the leucocyte, before its natural death within the body. In the alexin theory of immunity of Buchner and Hankin, an important part is assigned to the oxyphilic leucocytes in the production of these substances (alexins), which are supposed to paralyze bacterial activity and so to permit of phagocytosis. The excellent article on the pathology of infection by Kant-

hack in Allbutt's *System of Medicine* goes into this question most thoroughly.

The oxyphiles in the blood have been observed to be increased in number in several diseases, notably leucocythæmia and asthma. With the former we will not concern ourselves.

Müller (2) first noted the fact that the oxyphiles in the blood are increased in number in bronchial asthma. Many observers have confirmed this observation, among them Gollasch (3), Fink (4), Schwerchewski (5), Zappert (6), and Gabritschewski (7). Gabritschewski found twenty-five per cent. and thirty-three and a third per cent. of the leucocytes to be oxyphilic in two of his cases. He states that they are more numerous at the time of the attack. Schwerchewski, who noted 15.9 per cent. of oxyphiles in one of his cases, makes the same statement, and also that the onset of an attack can be foretold by the increase in oxyphiles which takes place some time previously. Zappert noted 8.77 per cent. and 12.36 per cent. of oxyphiles in the blood in cases of bronchial asthma.

The fact that the leucocytes in the sputum of persons suffering from bronchial asthma are largely oxyphilic has been noted by von Noorden (8), Leyden (9), Schmidt (10), Seifert (11), Fink (*loc. cit.*), and others. Charcot-Leyden crystals are also found in such sputum, and the relation between these crystals and the oxyphilic leucocytes is evidently a very close one. These crystals are found also in leucæmic blood where the oxyphilic leucocytes are present in large numbers. Fink (*loc. cit.*) found sixty-five per cent. of the leucocytes in asthmatic sputum to be oxyphilic, and the blood in the same case showed 14.6 per cent. of oxyphiles. The case here reported confirms all the above-quoted statements. The number of

oxyphiles in the blood (53.6 per cent.) was greater than in any other case I have been able to find in the literature of the subject. The great number of this form of leucocyte and of Charcot-Leyden crystals in the sputum was also very striking. The oxyphiles in the blood, while relatively greatly increased in number, of course bear a small relation to the total number of corpuscles (red and white), the proportion being about 1 to 1,122. This is sufficient reason for our not finding the Charcot-Leyden crystals in the dried specimens. An increase in the number of the oxyphilic leucocytes in the blood of syphilitics has been noted by several observers. No observation of more than ten per cent. has been recorded, however. The question as to the source of this increase in the number of oxyphilic leucocytes in the blood in asthma is an unsettled one. Gabritschewski (*loc. cit*) holds that the ordinary polynuclear leucocyte, which under normal conditions forms from sixty to eighty per cent. of the total number of all the forms in the blood, undergoes a pathological alteration of its protoplasm which, from being finely granular and neutrophilic, becomes coarsely granular and oxyphilic. Leyden (*loc. cit.*), on the other hand, holds that the oxyphilic leucocytes are the result of local new formation—*i. e.*, they are formed in the mucous membrane of the bronchioles.

Excellent general articles on the oxyphilic leucocytes are those of Zappert (*loc. cit.*), Neusser (12), and Schwarze (13).

Turning now to the question of chloro-anæmia, we find that many observers have noted this condition in syphilis.

Laache (14) first described the anæmia of syphilitics. Among the numerous observers who have investigated

this subject are Luzet (15), Scheff (16), Bergrun and Monti (17), and Loos (18). Many of them found the anæmia to resemble markedly that seen in chlorosis. In the latter disease the anæmia is not due so much to a decrease in the number of the red corpuscles as to a still more advanced reduction of the amount of hæmoglobin in each red corpuscle. In an ordinary secondary anæmia there is no reduction in the amount of hæmoglobin in each corpuscle; only the number of the corpuscles is reduced, so that the percentage of hæmoglobin sinks only as low (relatively) as the number of red corpuscles. In chlorosis and chloro-anæmia however, the hæmoglobin is relatively far below the red corpuscles; indeed, the number of the latter may be nearly normal and yet the anæmia be most marked. In our case the hæmoglobin was sixty-five per cent. and the number of red corpuscles 4,000,000 per cubic millimetre. The hæmoglobin is relatively much lower than the number of corpuscles, and to correspond with 4,000,000 corpuscles per cubic millimetre should be at least eighty per cent.

Loos (*loc. cit.*) draws attention to the fact that the blood in anæmia due to hereditary syphilis very often shows the presence of nucleated red corpuscles and of polychromatophilic red corpuscles. Examples of both of these abnormal elements were observed in the blood in the case here reported.

The nucleated red corpuscles were always normoblasts—*i. e.*, of the same size and shape as a normal red corpuscle, and showing the same staining qualities, but possessing a round nucleus, a fourth to a fifth the size of the corpuscle, which stained very deeply. The presence of such corpuscles in the blood is evidence of increased new formation of red corpuscles. Such new for-

mation is brought about by a preceding degeneration or destruction of red corpuscles, the demand upon the blood-forming organs for new red corpuscles being so great that immature normoblasts appear in the circulation. The so-called polychromatophilic red corpuscles are corpuscles which, when stained with Ehrlich's acid hæmatoxylin-eosin, take on a violet color instead of a bright red, the normal red corpuscles being stained the last-named hue. The presence of such corpuscles in the blood was at first held to be evidence of degeneration (Ehrlich (19)), but more recent investigations (Gabritschewski, *loc. cit.*) tend to show that they are evidence of regeneration rather than degeneration. The principal argument in favor of this view is the fact that the hæmoglobin of many of the nucleated red corpuscles seen in the blood in pernicious anæmia exhibits this polychromatophilic staining reaction. Lack of space forbids any discussion of the interesting reaction which the red corpuscles and hæmoglobin in the blood of syphilitics are said to undergo under the influence of mercury, and which Justus (20) thinks to be of great diagnostic value.

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